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IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF ARIZONA

Rowpar Pharmaceuticals, Inc., an Arizona Corporation, and Micropure, Inc., a Nevada Corporation, Plaintiffs, v. Lornamead, Inc., a Delaware Corporation, Defendant.	No. CV **COMPLAINT**

PLAINTIFFS ROWPAR PHARMACEUTICALS, INC. AND MICROPURE, INC., STATE AND ALLEGE AS FOLLOWS:

INTRODUCTION

1. This case is about misappropriation of trade secrets, breach of contract, and patent infringement by Lornamead, Inc. ("Lornamead").

2. Rowpar Pharmaceuticals, Inc. ("Rowpar") developed over many years the proprietary technology underlying its unique fluoride toothpaste known as ClōSYS® Sulfate-Free Fluoride Toothpaste, which includes the key ingredient of stabilized chlorine dioxide.

3. Recently, Rowpar approached Lornamead to explore the possibility of Lornamead acting as a contract manufacturer of Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste.

4. Rowpar disclosed to Lornamead, under the protection of confidentiality provisions in two distinct contracts, its detailed trade secrets concerning the manufacturing procedures and formulation for Rowpar's product.

5. Now, only six months later, Rowpar has discovered that Lornamead is using Rowpar's trade secrets to manufacture a copy of Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste, and is competing directly with Rowpar by selling that product under private label to Rowpar's largest customer.

6. Lornamead's improper conduct constitutes misappropriation of trade secrets, breach of two contracts, and infringement of at least one patent. Lornamead's audacious acts also threaten immediate irreparable harm to Rowpar, warranting prompt injunctive relief.

THE PARTIES

7. Plaintiff Rowpar Pharmaceuticals, Inc. ("Rowpar") is an Arizona Corporation having its principal place of business at 16100 N. Greenway-Hayden Loop, Suite F400, Scottsdale, Arizona, 85260-1789.

8. Plaintiff Micropure, Inc. ("Micropure") is a Nevada Corporation having its principal place of business in Scottsdale, Arizona. Micropure is a wholly owned subsidiary of Rowpar.

9. On information and belief, Defendant Lornamead, Inc., which also does business as Lornamead NA (collectively, "Lornamead") is a Delaware Corporation having its principal place of business at 500 Mamaroneck Avenue, Suite 104, Harrison, NY 10528. On information and belief, Lornamead has a manufacturing facility located at 175 Cooper Ave, Tonawanda, NY 14150, at which facility Lornamead produces toothpastes.

SUBJECT MATTER JURISDICTION

10. This Court has diversity jurisdiction over this case pursuant to 28 U.S.C. § 1332. The parties are completely diverse and the amount in controversy exceeds $75,000, exclusive of interest and costs.

11. In addition, this case arises in part under the patent laws of the United States, 35 U.S.C. § 1 et seq. Accordingly, the Court has subject matter jurisdiction over the patent infringement claims pursuant to 28 U.S.C. § 1331 and 1338.

12. This Court also has supplemental jurisdiction of the non-patent infringement claims pursuant to 28 U.S.C. § 1367.

PERSONAL JURISDICTION AND VENUE

13. This Court has personal jurisdiction over Lornamead because Lornamead has had substantial and continuous contacts with the State of Arizona relating to this case.

14. Lornamead purposefully sent senior representatives of the firm to Scottsdale, Arizona, to solicit business from Rowpar, and has made substantial contacts with Rowpar in Arizona by negotiating and entering into the contracts-at-issue in this case.

15. Moreover, Lornamead purposefully made substantial contacts with Rowpar in Arizona by arranging to receive trade secrets of Rowpar under the confidentiality obligations of the contracts-at-issue in this case.

16. In using Rowpar's trade secrets, Lornamead has manufactured products that were created using Rowpar's trade secrets and sold those products for distribution in Arizona. Those products have been sold within this judicial district through established distribution channels known to Lornamead.

17. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391(b) and 1400(b).

BACKGROUND

I. Rowpar and Its ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets

18. Rowpar is a company dedicated to providing innovative oral health solutions. The founder of Rowpar, Dr. Perry Ratcliff, discovered that stabilized chlorine dioxide could be used in personal oral care products for, among other benefits, reducing the level of harmful bacteria associated with bad breath and enhancing the health of the user. Rowpar's innovative products include specialty toothpaste, mouth rinse, breath spray, and dental unit water cleaner.

19. Dr. Ratcliff's innovative work also led to more than twenty U.S. Patents and patent applications, including U.S. Patent Number 6,017,554.

20. Rowpar introduced its first toothpaste product in about 1993. That product was a fluoride-free, sulfate-free toothpaste containing stabilized chlorine dioxide. Rowpar continued its research and development work after this initial product offering, in an effort to improve that product and develop new innovative toothpaste products.

21. Chlorine dioxide is an inherently unstable substance that tends to dissipate rapidly in solution. It also tends to react with other ingredients found in toothpaste. As a result, developing and manufacturing a stable, consistent, and commercially viable product such as toothpaste containing both stabilized chlorine dioxide and fluoride is not a simple endeavor.

22. Rowpar's newest toothpaste product is called ClōSYS® Sulfate-Free Fluoride Toothpaste. It contains stabilized chlorine dioxide as well as sodium fluoride. Rowpar's development work on ClōSYS® Sulfate-Free Fluoride Toothpaste spanned more than five years, and involved substantial research, experimentation and refinement of both the product formulation and the commercial manufacturing process, all in an effort to achieve an optimal product and an optimal process for commercial production.

23. ClōSYS® Sulfate-Free Fluoride Toothpaste is not merely the prior ClōSYS® toothpaste with the addition of a fluoride source. Developed under contract with the University of Iowa School of Pharmacy and tested by the Indiana University School of Dentistry, it has been shown to surpass the industry standard in promoting remineralization and inhibiting demineralization of teeth. Further, the addition of sodium fluoride source to a toothpaste with stabilized chlorine dioxide substantially alters the taste and consumer goodness qualities of the product, requiring special flavoring to the product to achieve consumer goodness qualities. But chlorine dioxide is a powerful oxidizing agent that attacks most flavoring agents, so it was also necessary for Rowpar to invest in and develop means to flavor its ClōSYS® Sulfate-Free Fluoride Toothpaste, making it a unique and highly desirable product.

24. Introduced in early 2011, ClōSYS® Sulfate-Free Fluoride Toothpaste has quickly become Rowpar's top-selling toothpaste among dental professionals and consumers.

25. In developing its ClōSYS® Sulfate-Free Fluoride Toothpaste and the associated manufacturing process, Rowpar has accumulated and taken reasonable efforts to protect the confidentiality of a significant body of valuable proprietary and/or trade secret information associated with the formulation and production of ClōSYS® Sulfate-Free Fluoride Toothpaste.

26. While Rowpar has disclosed certain aspects of how to make and use a fluoride-based chlorine dioxide toothpaste in its patent applications, Rowpar has never disclosed the specific formula and manufacturing process for its commercialized ClōSYS® Sulfate-Free Fluoride Toothpaste. The specific formulation for ClōSYS® Sulfate-Free Fluoride Toothpaste is unique and a closely held and valuable trade secret of Rowpar. Similarly, the manufacturing process for ClōSYS® Sulfate-Free Fluoride Toothpaste is unique and a closely held and valuable trade secret of Rowpar.

27. Rowpar maintains the confidentiality of its proprietary and confidential information associated with its ClōSYS® Sulfate-Free Fluoride Toothpaste by, among other things: (a) labeling documents "Confidential" as appropriate; (b) requiring employees to sign employment agreements that contain confidentiality and non-disclosure obligations; (c) restricting access to confidential documents; (d) implementing physical and digital security measures; (e) executing non-disclosure agreements with third parties; and (f) following an appropriate exit interview protocol.

28. Rowpar has from time-to-time enlisted other companies or Universities to provide testing, evaluation, or other research services on a contract basis. When other companies have provided such services to Rowpar, those services were performed under obligations of confidentiality to Rowpar.

29. In addition, Rowpar contracts with other companies to act as contract manufacturers for Rowpar. Such contractors may be primary manufacturers or, to ensure continuity of supply, backup manufacturers. When other companies have agreed

to provide manufacturing services to Rowpar, those services have been performed under obligations of confidentiality to Rowpar.

II. Lornamead Signs a Master Supplier Agreement Obligating Lornamead to Confidentiality and Not Misusing Rowpar's Trade Secrets

30. In 2006, Lornamead and Rowpar entered into a Master Supplier Agreement.

31. The Master Supplier Agreement became effective on December 29, 2006, and it remains in full force and effect at the present time.

32. Among other terms, the Master Supplier Agreement obligates Lornamead to not disclose or use any confidential information of Rowpar for any purpose other than to quote and/or supply products to Rowpar.

33. According to paragraph 13.1 of the Master Supplier Agreement, Lornamead is "accountable and liable to Rowpar for any unauthorized disclosure or misuse" of Rowpar's confidential information.

34. According to its terms, the Master Supplier Agreement terminates and supersedes any and all prior agreements and understandings between Rowpar and Lornamead.

35. For a time, Lornamead acted as a primary manufacturer of Rowpar's fluoride-free toothpaste product pursuant to the Master Supplier Agreement. Rowpar, however, stopped ordering product from Lornamead in about March 15, 2011. The Master Supplier Agreement, however, remains in effect.

36. Even though Rowpar stopped ordering product from Lornamead, Lornamead continued to solicit business from Rowpar from time to time.

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III. Lornamead Signs a Bilateral Confidentiality and Non-Analysis Agreement Further Obligating Lornamead to Confidentiality and Not Misusing Rowpar's Trade Secrets

37. In October 2012, Rowpar decided to seek an additional manufacturer for its ClōSYS® Sulfate-Free Fluoride Toothpaste. Lornamead indicated an interest in that work. To that end, on October 22, 2012, Rowpar and Lornamead executed a contract entitled "Bilateral Confidentiality and Non-Analysis Agreement" ("BCNA Agreement").

38. In the BCNA Agreement, Lornamead undertook the following obligations with respect to Rowpar's confidential information:

"a) to hold the Confidential Information on a confidential basis as if it were its own Confidential Information;

b) to refrain from using the Confidential Information either directly or indirectly for any other purpose other than for the achievement of the Project; [and]

c) to limit the disclosure of the Confidential Information to its directors and employees who need to have access to said information in the course of the Project, [Lornamead] ensuring from its directors and employees the same obligation of confidentiality and remaining liable for any breach by them of the terms and conditions contained hereunder. . . ."

39. The BCNA Agreement defined "Confidential Information" to be "information of any kind, such as technical, financial, and commercial" information, which "may include without limitation, patent, know-how, formulae, processes, designs, sketches, schemes, models, plans, samples, inventions, ideas, research and development programs, business data specifications, and/or technical and commercial data."

40. According to Article 6 of the BCNA Agreement, Lornamead agreed to indemnify Rowpar and hold Rowpar harmless from "any and all losses, (including

reasonable lawyers' fees) caused by or arising from any breach of the confidentiality obligations contained in this Agreement."

41. Furthermore, according to Article 6 of the BCNA Agreement, the Receiving Party (Lornamead) "recognises [sic] that breach of this Agreement may cause to the Disclosing Party [Rowpar] irreparable harm and that monetary relief will not adequately compensate the Disclosing Party [Rowpar] for its losses. The Disclosing Party [Rowpar] shall be entitled to equitable relief, including specific performance, for any breach of this Agreement by the Receiving Party [Lornamead], in addition to all other available remedies."

IV. Rowpar Discloses Its Core Trade Secrets to Lornamead.

42. On November 9, 2012, after execution of the BNCA Agreement, Rowpar transmitted to Lornamead the manufacturing specifications for its ClōSYS® Sulfate-Free Fluoride Toothpaste. The transmittal was marked "Confidential," as was each page of the specifications document.

43. Also after execution of the BNCA Agreement, Rowpar had additional communications with Lornamead during which further confidential and trade secret information about Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste formulation and manufacturing process was disclosed.

44. The manufacturing specification for Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste includes the product formulation, and provides detailed identification of each component used and the quantity needed. It also includes step-by-step instructions and know-how regarding how to manufacture Rowpar's fluoride-based chlorine dioxide toothpaste. It is the product of years of research, experimentation, refinement, and analysis. Rowpar has taken reasonable efforts to maintain its secrecy. It has significant value by reason of its secrecy.

45. The manufacturing specification for Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste is one of Rowpar's core trade secrets.

46. Had Rowpar not obtained contractual promises from Lornamead that Lornamead would not use the manufacturing specification for any purpose other than becoming a backup manufacturer to Rowpar, Rowpar would not have sent the manufacturing specification to Lornamead. Certainly, the use by Lornamead of this information to produce a competing copy of Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste is wholly unauthorized and in direct violation of Rowpar's reasonable expectations and Lornamead's contractual obligations.

V. Lornamead Misuses Rowpar's Trade Secrets to Produce a Copy Cat Product

47. Less than six months after Rowpar disclosed its highly confidential manufacturing specifications and product formulation to Lornamead, Rowpar discovered that Lornamead had begun manufacturing a sulfate-free stablilized chlorine dioxide toothpaste with fluoride that is materially identical to Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste, and selling that copy-cat product in direct competition with Rowpar, to Rowpar's largest customer.

48. On information and belief, one week after receiving the manufacturing specification for Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste, Lornamead submitted on November 15, 2012 a "Secure Product Listing" for its sulfate-free chlorine dioxide toothpaste to the federal Food and Drug Administration (FDA). Attached to the Secure Product Listing were images of the labels for the tube of sulfate-free chlorine dioxide toothpaste and the box in which the toothpaste is sold.

49. Later, and as discussed further below, Rowpar discovered that these same labels appear on the toothpaste being sold side-by-side with Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste at Walgreens stores within Arizona and across the

country under the name "Anticavity Sulfate-Free Fluoride Toothpaste," in association with the phrase "Well at Walgreens" (hereinafter, "Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste").

50. The Secure Product Listing submitted to the FDA lists the "establishment" responsible for "manufacturing" and "pack[aging]" Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste as "Lornamead."

51. Lornamead is the "Registrant" to the FDA for Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste.

52. The ingredient list on the label of Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste is identical to the ingredient list on Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste.

a. The ingredient list on label of Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste lists Sodium Fluoride 0.24% (w/w) as the sole active ingredient. It also lists the following inactive ingredients: water, hydrated silica, sorbitol, stabilized chlorine dioxide, cellulose gum, dibasic sodium phosphate, titanium dioxide, sodium phosphate, and sucralose.

b. The ingredient list on the label of Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste lists Sodium Fluoride 0.24% (w/w) as the sole active ingredient. It also lists the following inactive ingredients: water, hydrated silica, sorbitol, stabilized chlorine dioxide, cellulose gum, dibasic sodium phosphate, titanium dioxide, sodium phosphate, and sucralose.

53. On information and belief, Lornamead could not have, and did not, develop and manufacture its copy-cat product without using trade secrets and confidential information of Rowpar.

54. Accordingly, Lornamead without authorization has used, and continues to use, Rowpar's trade secrets and confidential information about ClōSYS® Sulfate-Free

Fluoride Toothpaste, including without limitation Rowpar's manufacturing specification and product formulation.

VI. Lornamead's Improper Conduct is Causing Irreparable Harm to Rowpar

55. Lornamead is selling its copy of Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste under private label to Rowpar's largest customer, Walgreens. It is available for purchase in Walgreens stores within Arizona and across the country under the name "Anticavity Sulfate-Free Fluoride Toothpaste," in association with the phrase "Well at Walgreens."

56. The packaging of Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste states, "Compare to ClōSYS® active ingredient," thereby encouraging consumers to notice the near-identity of the products.

57. Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste is placed in Walgreen's stores in Arizona side-by-side with Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste, on the same shelf.

58. Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste product is priced drastically lower than Rowpar's ClōSYS® Fluoride Toothpaste.

59. Rowpar has been damaged by Lornamead's unauthorized use of Rowpar trade secrets and confidential information in the manufacture and sale of Lornamead's sulfate-free, stabilized chlorine dioxide toothpaste with fluoride. That damage is ongoing, continuous, and in large part irreparable.

60. The sale of Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste is irreparably harming Rowpar by, among other things, irreparably tarnishing the goodwill and business reputation among consumers and dental professionals that Rowpar has painstakingly earned over many years as an innovative source of premium oral health products. In addition, Lornamead's unfair competition is impairing in

irreparable, unquantifiable ways the market for, and commercial value of, ClōSYS® Sulfate-Free Fluoride Toothpaste as well as other Rowpar products.

FIRST CAUSE OF ACTION:
MISAPPROPRIATION OF TRADE SECRETS
(*Arizona Uniform Trade Secrets Act, Ariz. Rev. Stats., § 44-401 et seq.*)

61. Rowpar realleges and incorporates by reference the allegations in paragraphs 1 - 60 of this Complaint.

62. Rowpar possesses trade secrets relating to its ClōSYS® Sulfate-Free Fluoride Toothpaste, with respect to its formulation and manufacturing process (hereinafter, "ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets"). Said trade secrets include, without limitation, the information contained in Rowpar's manufacturing specification for its ClōSYS® Sulfate-Free Fluoride Toothpaste.

63. The ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets constitute trade secrets as defined in the Arizona Uniform Trade Secrets Act, § 44-401.

64. The ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets have and continue to derive independent economic value from that information not being generally known and not being readily ascertainable by proper means by other persons who can obtain economic value from its disclosure and/or use.

65. Rowpar has made reasonable efforts under the circumstances to maintain the secrecy of the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets.

66. Lornamead acquired and used the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets and knew, or had reason to know, that the trade secrets were acquired and used by improper means, without authorization, and in violation of Arizona's Uniform Trade Secrets Act.

67. At the time Lornamead used the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets to produce Lornamead's sulfate-free fluoride-based chlorine

dioxide toothpaste, Lornamead knew or had reason to know that its knowledge of the ClōSYS® Sulfate-Free Fluoride Trade Toothpaste Trade Secrets was acquired under circumstances giving Lornamead a duty to limit Lornamead's use of the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets.

68. Lornamead used the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets in excess of the uses permitted under the Master Supplier Agreement.

69. Lornamead used the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets in excess of the uses permitted under the BCNA Agreement.

70. Accordingly, Lornamead was not authorized to use the ClōSYS® Fluoride Toothpaste Trade Secrets to produce Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste.

71. By using the ClōSYS® Fluoride Trade Secrets without authorization to produce Lornamead's sulfate-free fluoride-based chlorine dioxide toothpaste, Lornamead misappropriated the ClōSYS® Sulfate-Free Fluoride Trade Secrets.

72. Rowpar has suffered and is suffering actual losses from Lornamead's misappropriation of the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets.

73. Lornamead has been and is being unjustly enriched by its misappropriation of the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets.

74. Lornamead's misappropriation of the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets has caused and is causing Rowpar to suffer money damages.

75. Lornamead's misappropriation of the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets has caused and is causing Rowpar irreparable injury not compensable by money damages.

76. Lornamead's conduct constitutes willful and malicious misappropriation of the ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets, entitling Rowpar to exemplary damages and attorney's fees.

77. Rowpar has been and continues to be irreparably harmed such that a remedy at law is inadequate and preliminary and permanent injunctive relief is necessary.

SECOND CAUSE OF ACTION:
BREACH OF CONTRACT OF MASTER SUPPLIER AGREEMENT

78. Rowpar realleges and incorporates by reference the allegations in paragraphs 1 - 77 of this Complaint.

79. At all relevant times, the Master Supplier Agreement was and is a valid and enforceable contract.

80. By, among other conduct, using Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets for a purpose other than to supply toothpaste to Rowpar, Lornamead breached the Master Supplier Agreement.

81. As a result of the breach, Rowpar has been and continues to be damaged.

82. As a result of the breach, Rowpar is suffering ongoing irreparable harm such that preliminary and permanent injunctive relief is necessary.

THIRD CAUSE OF ACTION:
BREACH OF CONTRACT OF BCNA AGREEMENT

83. Rowpar realleges and incorporates by reference the allegations in paragraphs 1 - 82 of this Complaint.

84. At all relevant times, the BCNA Agreement was and is a valid and enforceable contract.

85. By among other conduct, using Rowpar's ClōSYS® Sulfate-Free Fluoride Toothpaste Trade Secrets for a purpose other than to supply toothpaste to Rowpar, Lornamead breached the BCNA Agreement.

86. As a result of the breach, Rowpar has been and continues to be damaged.

87. Under the terms of the BCNA Agreement, Rowpar is entitled to injunctive relief arising from a breach of Lornamead's confidentiality obligations pursuant to the BCNA Agreement.

88. Under the terms of the BCNA Agreement, Rowpar is entitled recover from Lornamead all losses, including reasonable attorneys fees, arising from a breach of Lornamead's confidentiality obligations pursuant to the BCNA Agreement.

89. As a result of the breach, Rowpar has been and continues to be damaged.

90. Under the terms of the BCNA Agreement, Rowpar has been irreparably harmed by a breach of the BCNA Agreement such that monetary relief will be inadequate to compensate Rowpar.

91. As a result of the breach, Rowpar is suffering ongoing irreparable harm such that preliminary and permanent injunctive relief is necessary.

FOURTH CAUSE OF ACTION:
INFRINGEMENT OF U.S. PATENT 6,017,554

92. Rowpar realleges and incorporates by reference the allegations in paragraphs 1 - 91 of this Complaint.

93. On January 25, 2000, United States Patent No. 6,017,554 ("the '554 patent"), entitled "Composition for Treating Abnormal Conditions of the Epithelium of Bodily Orifices" was duly and legally issued by the United States Patent and Trademark Office. A true and correct copy of the '554 patent is attached as Exhibit A to this Complaint.

94. Micropure was assigned and continues to hold and right, title, and interest in the '554 patent.

95. On information and belief, Lornamead makes, uses, offers to sell, and/or sells in the United States stabilized chlorine dioxide toothpastes, including, for example, the Anticavity Sulfate-Free Toothpaste it sells to Walgreens, that infringe at least one

claim of the '554 Patent. Accordingly Lornamead has been and is infringing the '554 patent in violation of 35 U.S.C. § 271(a).

96. Lornamead's acts of infringement have caused and continue to cause damage to Rowpar and Micropure, and Rowpar and Micropure are entitled to recover from Lornamead the damages sustained by Rowpar in an amount to be proven at trial.

97. Lornamead's infringement has and will continue to irreparably harm Rowpar unless and until such infringement is enjoined by this Court.

FIFTH CAUSE OF ACTION:
ENTITLEMENT TO PRELIMINARY AND PERMANENT INJUNCTIVE RELIEF

98. Rowpar realleges and incorporates by reference the allegations in paragraphs 1 - 97 of this Complaint.

99. Rowpar has a strong likelihood of success on its claims against Lornamead.

a. Rowpar has a strong likelihood of success on its claim of misappropriation of trade secrets against Lornamead.

b. Rowpar has a strong likelihood of success on its claim of breach of contract of the Master Supplier Agreement against Lornamead.

c. Rowpar has a strong likelihood of success on its claim of breach of contract of the BCNA Agreement against Lornamead.

100. Rowpar has been and is being irreparably harmed by Lornamead's continuing use of Rowpar's trade secrets.

101. The balance of harms strongly tips in favor of granting an injunction.

a. CloSYS® Fluoride Toothpaste is Rowpar's best selling product.

b. Rowpar, not Lornamead, developed the formula for a fluoride-based chlorine dioxide toothpaste.

c. Lornamead is using Rowpar's formula to co-opt Rowpar's relationship with its largest customer, Walgreens.

d. Lornamead's diversion of Rowpar's sales is likely to impact Rowpar's sales of its other chlorine dioxide products, including its oral rinse.

102. The public interest favors an injunction.

a. Rowpar has sufficient capacity to meet market demand for fluoride-based chlorine dioxide toothpaste.

b. The public interest in promoting fair competition in the marketplace favors an injunction.

WHEREAS, Rowpar and Micropure respectfully requests that the Court:

A. Enter judgment that Lornamead

i. misappropriated the trade secrets of Rowpar, in violation of the Arizona Trade Secrets Act, Ariz. Rev. Stats., § 44-401 et seq.,

ii. breached the Master Supplier Agreement,

iii. breached the BCNA Agreement, and

iv. infringed the '554 patent;

B. Award Rowpar damages sufficient to compensate it for Lornamead's misappropriation of Rowpar's trade secrets, breach of the Master Supplier Agreement, breach of the BCNA Agreement, and infringement of the '554 patent;

C. Award Rowpar its attorneys' fees incurred in this action pursuant to a declaration that Lornamead's misappropriation of Rowpar's trade secrets was willful and malicious, the terms of the BCNA Agreement, Ariz. Rev. Stat. § 12-341.01 titled "Recovery of Attorneys' Fees," and a declaration that this case is exceptional under 35 U.S.C. § 285;

D. Award Rowpar exemplary damages under the Arizona Uniform Trade Secrets Act pursuant to a declaration that Lornamead's misappropriation of Rowpar's trade secrets was willful and malicious;

E. Award Rowpar pre-judgment and post-judgment interest and costs;

F. Preliminarily and Permanently Enjoin Lornamead's use of Rowpar's trade secrets, breach of the Master Supplier Agreement, breach of the BCNA Agreement, and infringement of '554 patent;

G. Order Lornamead to return to Rowpar any and all confidential information and trade secret information disclosed to Lornamead by Rowpar; and

H. Award Rowpar such other relief as the Court deems just and equitable.

DEMAND FOR JURY TRIAL

Rowpar respectfully requests a jury trial on any and all issues for which a jury trial is permitted under applicable law.

DATED this 28th day of May, 2013.

GUST ROSENFELD, PLC

/s/ Timothy J. Watson – 018685
Richard B. Hood
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Attorneys for Plaintiffs

Exhibit A

US006017554A

United States Patent [19]

Ratcliff

[11] Patent Number: 6,017,554

[45] Date of Patent: Jan. 25, 2000

[54] **COMPOSITION FOR TREATING ABNORMAL CONDITIONS OF THE EPITHELIUM OF BODILY ORIFICES**

[75] Inventor: **Perry A. Ratcliff**, Scottsdale, Ariz.

[73] Assignee: **Micropure, Inc.**, Scottsdale, Ariz.

[21] Appl. No.: **09/189,782**

[22] Filed: **Sep. 21, 1998**

Related U.S. Application Data

[62] Division of application No. 08/831,931, Apr. 2, 1997, Pat. No. 5,811,115, which is a continuation of application No. 08/444,550, May 19, 1995, Pat. No. 5,618,550, which is a division of application No. 08/087,606, Jul. 6, 1993, Pat. No. 5,489,435.

[51] **Int. Cl.**[7] **A61K 9/00**; A61K 33/00

[52] **U.S. Cl.** **424/422**; 424/422; 424/45; 424/49; 424/52; 424/53; 424/57; 424/78.02; 424/427; 424/434; 424/437; 424/430; 424/661; 424/673; 424/676; 424/DIG. 15; 514/944; 514/945; 514/966; 514/967; 514/968

[58] **Field of Search** ..... 424/45, 49, 52, 424/53, 57, 78.02, 427, 434, 437, 430, 661, 673, 676, DIG. 15; 514/944, 945, 966, 967, 968

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[57] **ABSTRACT**

A stable solution cream, salve, or spray composition containing activated stabilized chlorine dioxide and phosphates, such as disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, and sodium monofluorophosphate, is disclosed for the prevention and treatment of abnormal conditions of the epithelium of bodily orifices. Examples of such abnormal conditions of the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices include bacterial infections, such as *Actinobacillus actinomycetemcomitans* and *Porphyromonoas gingivalis,* and fungal infections, such as Candida, and leukoplakia. The preferred concentration ranges are between about 0.005%–2.0% chlorine dioxide, and between about 0.02%–3.0% phosphate. The phosphate compound retards escape of chlorine dioxide in the pH range of 6.0 to 7.4, at which pH stabilized chlorine dioxide becomes activated and releases sufficient chlorine dioxide to reduce motility and become lethal to the involved micro-organisms.

15 Claims, No Drawings

COMPOSITION FOR TREATING ABNORMAL CONDITIONS OF THE EPITHELIUM OF BODILY ORIFICES

This is a divisional of application of Ser. No. 08/831,931 filed on Apr. 2, 1997 now Pat. No. 5,811,115, which is a continuation application of Ser. No. 08/444,500 filed May 19, 1995 now Pat. No. 5,618,550, which is a divisional application of Ser. No. 08/097,606, filed Jul. 6, 1993 now Pat. No. 5,489,435.

BACKGROUND OF THE INVENTION

The present invention is directed to a method and composition for prevention and treatment of abnormal conditions of the epithelium of bodily orifices. More particularly, the present invention relates to the use of activated stabilized chlorine dioxide in conjunction with a phosphate compound (to provide stability and as a surfactant or nonsudsing detergent to reduce surface tension on mucosal tissues assisting in the exposure of the epithelial covering to the activated chlorine dioxide), to thereby prevent and treat fungal and bacterial infections of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices, and other abnormal conditions of the epithelium, including leukoplakia.

Thiols, particularly the volatile sulfur compounds such as hydrogen sulfide, methylmercaptan and dimethylsulfide, are recognized in the current literature as being major contributors to the penetration of bacterial toxins through the epithelial barrier into the underlying basal lamina and connective tissue. A. Rizzo, Peridontics, 5:233–236 (1967); W. Ng and J. Tonzetich, J. Dental Research, 63(7):994–997 (1984); M. C. Solis-Gaffar, T. J. Fischer and A. Gaffar, J. Soc. Cosmetic Chem., 30:241–247 (1979); I. Kleinberg and G. Westbay, J. Peridontol, 63(9): 768–774 (1992). The penetration of this barrier makes possible the invasion of antigenic substances such as viral and bacterial toxins and bacteria into the underlying substrate. Thus, by removing the volatile sulfur compounds and maintaining the epithelial barrier there is a reduction in the penetration capacity of antigens and microbiota (A. Rizzo, Peridontics, 5:233–236 (1967); W. Ng and J. Tonzetich, J. Dental Research, 63(7): 994–997 (1984); M. C. Solis-Gaffar, T. J. Fischer and A. Gaffar, J. Soc. Cosmetic Chem., 30:241–247 (1979)) as well as the destruction of the motility and the death of bacterial and viral forms.

Studies done in the mouth have demonstrated that the penetration of bacteria takes place in the presence of the volatile sulfur compounds, resulting in initiation of the inflammatory reaction including initiation of the complement cascade. I. Kleinberg and G. Westbay, J. Peridontol, 63(9): 768–774 (1992). Initiation of the inflammatory reaction and development of the complement leads to an eightfold increase in the cell division or mitosis of epithelial cells in the attachment apparatus of the gingiva. W. O. Engler, S. P. Ramfjiord and J. J. Hiniker, J. Periodont., 36:44–56 (1965). Because the epithelia of other orifices, and particularly vaginal epithelium, are very similar to the gingival epithelium, reactions similar to those described above for the gingival epithelium occur in all other parts of the body, as demonstrated by the occurrence of vaginitis and endometriosis of the vagina. Examples of such bacteria which may appear in any bodily orifice include *Porphyromonas* (formerly known as Bacteroides) *gingivalis, Actinobacillus actinomycetemcomitans*, and Pseudomonades.

The volatile sulfur compounds are generated primarily from the polypeptide chains of the epithelial cell walls, and

from the cell walls, pili, fimbrae, and flagella of microorganisms, including fungi, that are part of the normal flora of the organs of the exposed surfaces of the body. The polypeptide chains are composed of a series of amino acids including cysteine, cystine, and methionine, each of which contain sulfur side chains. The death of the microorganisms or the epithelial cells results in degradation of the polypeptide chains into their amino acid components, particularly cysteine and methionine, which then become the source of the sulfur compounds hydrogen sulfide, methylmercaptan and di-methylsulfide which alter the epithelial barrier, permitting penetration of the barrier by antigenic substances.

Penetration of the epithelial barrier by volatile sulfur compounds reduces the capacity of the tissues to protect against bacteria, virus, fungus, and yeast forms. Tonzetich has shown, using S^{35}-labelled methylmercaptan, the penetration of thiol through the epithelium, plus the basal lamina, into the underlying connective tissues where it begins degradation of collagen fibers. W. Ng and J. Tonzetich, J. Dental Research, 63(7): 994–997 (1984). In addition, it is the nature of many of the bodily orifices that they are inhabited by both pathogenic and non-pathogenic organisms. If an antibiotic is used to reduce the organisms normally present, opportunistic yeast forms and other pathogenic organisms resistant to the administered antibiotic often invade or multiply at or in the bodily orifices.

Candida species, particularly *Candida albicans*, are the yeasts that primarily affect the mouth and the female vagina. In the mouth, infection by Candida is called Thrush; in the vagina it is called *vaginitis*.

With the increase of patients having immunocompromising diseases such as AIDS, leukemia, diabetes and immunosuppressing diseases such as stress, alcoholism, etc., a progressively higher percentage of the human population is susceptible to invasion and growth of bacterial and fungal Candida organisms. In addition, such patients are susceptible to the development of conditions of leukoplakia such as oral hairy leukoplakia and leukoplakia vulvae.

In patients afflicted with diabetes, as well as familial history diabetes, the neutrophil, which is the first line defense cell against foreign antigens, has an altered 110 Dalton surface protein which reduces the capacity of the neutrophil to phagocytize bacteria by approximately 50%. R. J. Genco, T. E. Van Dyke, M. J. Levine, R. D. Nelson and M. E. Wilson, J. Dental Research, 65(12):1379–1391 (1986). As a result of the development of antibiotics, insulin, and more sophisticated methods of treating diabetes, early deaths of diabetics from infections have been prevented, resulting in a several-fold increase in the number of familial history diabetes in the population. Thus, the increased presence of the diabetes gene in the gene pool of the human race is rapidly increasing, resulting in a higher number of humans with an immunocompromised capacity. This fact in part explains why some women develop vaginitis whenever they are treated with antibiotic drugs.

STABILITY OF CHLORINE DIOXIDE

Chlorine dioxide is unstable in aqueous solutions at lower pH levels. It is produced commercially and shipped in an aqueous solution in its hydrolytic byproduct forms at 8.3 to 9.0 pH. At that range there is complete retention of the chlorine dioxide hydrolyzed forms within the solution so that a shelf life of from 1–5 years may be achieved. When the pH of chlorine dioxide is lowered to 7.2 or below, chlorine dioxide begins to become activated and, in the gaseous form, it is available for reactivity with thiols, microorganisms, and organic debris in solution.

At present, there is an inadequate capacity of existing pharmaceutical drugs to control Candida infections (IADR symposium, March 1993). The severe diseases may be resistant to the commonly used drugs ketonideozole and nystatin, etc. Other synthetic drugs which are used systemically may have limited effects, and infections are resistant to treatment. Combinations of these drugs systemically and by suppositories may not always work.

In an in vitro study by the present inventor of Candida culture using the protocol of a simulated oral environment as stipulated by the Food and Drug Administration in the *Federal Register*, Vol. 47, No. 101 (May 25, 1982), wherein calf serum is added to the tryptic soy broth inoculated with the Candida, one ml. of the Candida culture was withdrawn and plate counted by standard techniques to determine the baseline content of the Candida population. Both a solution and a slurry of 1 ml. paste containing 0.1% chlorine dioxide with 0.2% phosphate stabilizer plus 2 ml. of distilled water was added to the TSB broth with calf serum. Additional samples were taken at 10, 30 and 60 seconds and again plated to count the remaining Candida. It was found that at 10 seconds there was a 99+% reduction of *Candida albicans* using standard plate count techniques.

In a six month clinical trial by the present inventor, samples were taken from the gingival crevice of the mouth. After treatment of humans with a composition comprising 0.10% chlorine dioxide and 0.2% phosphate stabilizer, the inventor showed by means of standard plate count methods that during the period from baseline to six months, there was a statistically significant reduction of *Candida albicans*. This clinical trial demonstrates the capacity of a composition comprising 0.1% activated stabilized chlorine dioxide together with metallic phosphate (the latter compound acting both to stabilize the chlorine dioxide solution and also as a surfactant to break the surface tension and allow chlorine dioxide to effectively interact with the *Candida albicans* infection) to prevent and treat the development of a Candida infection.

Further details of the preparation and use of chlorine dioxide/phosphate compositions can be found in U.S. Pat. No. 5,200,171, issued Apr. 6, 1993 to Ratcliff, which is hereby incorporated by reference.

SUMMARY OF THE INVENTION

Briefly, and in accord with one embodiment of the present invention, a composition containing stabilized chlorine dioxide and a phosphate is disclosed as being useful in preventing and treating abnormal conditions of the epithelium of bodily orifices. Examples of such abnormal conditions of the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices include bacterial and fungal infections, such as Candida, and leukoplakia. Stabilized chlorine dioxide is an effective agent for removing thiol compounds for deodorizing the mouth as well as deodorizing other bodily orifices, such as the vagina. The addition of activating inhibitor phosphates to the stabilized chlorine dioxide reduces surface tension and retards the rapid escape of chlorine dioxide gas at the pH range of 6.5 to 7.0 typical of orifices of the body. Preferred concentrations of stabilized chlorine dioxide compounds are in the range of between about 0.005% to 2.0%. The concentration of the phosphate compound, preferably disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, and sodium monofluorophosphate, is in the range of between about 0.02 to 3.0%.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Broadly, the present invention contemplates the use of an activating inhibitor and surface tension reducing agent, specifically, a phosphate compound, preferably, disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate (in particular, trisodium phosphate, or sodium monofluorophosphate), combined with a stabilized chlorine dioxide solution, to make possible the lowering of the pH of the mixture to an optimal value of less than about 7.2 at the time the mixture is used to prevent and treat abnormal conditions of the epithelium of bodily orifices, such as those caused by fungal and bacterial infections of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices, and other abnormal conditions of the epithelium, including leukoplakia.

The present invention can be used to control the above-described bodily orifice maladies in humans, and animals which are human companions, such as dogs, cats, horses, etc., by reducing the presence of fungal and bacterial infections and leukoplakia in bodily orifices of the human and animal population, to prevent transference and cross infection from person to person or animal to person or animal to animal. Thus, the present invention can be used in both human and veterinary applications.

Clinical observations and in vitro and in vivo studies by the inventor have led to the discovery that an activating inhibitor phosphate such as disodium monohydrogen phosphate, sodium dihydrogen phosphate, or, preferably, trisodium phosphate, or sodium monofluorophosphate, causes a reduction in surface tension, as well as stabilizing chlorine dioxide, so that the chlorine dioxide remains effective at a lower pH than was previously thought possible. In addition, the phosphate is a detergent which is used in place of other detergents for lowering surface tension and lo allowing the activated chlorine dioxide to become available to the convoluted surfaces of the body orifices. The preferred concentration ranges are between about 0.005%–2.0% chlorine dioxide, and between about 0.02%–3.0% phosphate. For most patients, the preferred concentration of chlorine dioxide will be in the range of between about 0.005–0.5%; in the case of extremely immunocompromised patients having runaway bacterial or fungal infections or severe leukoplakia, it is preferred to increase the concentration of chlorine dioxide up to about 1.0–2.0%.

The permeability of mucus epithelial tissue is increased substantially by exposure to thiol compounds including hydrogen sulfide (H_2S) and methylmercaptan (CH_3—SH) and dimethylsulfide (CH_3—S—CH_3). In a Candida infection, there is increased inflammation and degeneration of epithelial cells, which break down into thiols, including the above sulfur compounds. A vicious cycle is established, leading to an environment for the increase of Candida growth. If the patient is immunocompromised with AIDS, the problem is exacerbated with ulcerations that could increase the probability of sexually transmitted disease. Likewise, a non-AIDS patient could be more exposed to sexually transmitted disease.

The following examples further illustrate various features of the invention but are intended in no way to limit the scope of the invention which is defined in the appended claims.

EXAMPLE 1

The stability of Chlorine Dioxide at Ph 6.8 in the Presence of Phosphate.

Materials:

1. Purogene (2% $C10_2$), Lot #8907.41, 1 gallon, Manufactured by BIO-Cide, International, P.O. Box 2700, Norman, Okla. 73070.

2. Sodium Phosphate, monobasic, dibasic, and tribasic.

Methods:

A 10% solution of monobasic sodium phosphate was prepared in distilled water. Ten ml was placed into each of four beakers. One of each of the four beakers received 1, 2.5, 5, and 10 ml of chlorine dioxide concentrate (2% $C10_2$), respectively. All solutions were diluted to 90 ml with distilled water, adjusted to pH 6.8 with 1 N NaOH and 1 N HCl, diluted to 100 ml and placed in screw cap bottles.

Solutions containing dibasic and tribasic sodium phosphate and a distilled water blank control were prepared in a similar manner.

Chlorine dioxide content and pH was determined for each solution on days 0, 7, 14, 21 and 28 in accordance with Standard Methods for the Examination of Water and Wastewater, 17th edition, 1989.

Results and Summary:

As shown in Table 1, the content of chlorine dioxide was stable in all sodium phosphate solutions and distilled water control over the 28 day test period. The pH of all samples ranged from 6.1 to 7.6.

Solutions containing dibasic and tribasic sodium phosphate and a distilled water blank control are prepared in a similar manner.

Chlorine dioxide content and pH is determined for each solution on days 0, 7, 14, 21 and 28 in accordance with Standard Methods for the Examination of Water and Wastewater, 17th edition, 1989, in order to determine the stability of chlorine dioxide over time.

EXAMPLE 3

The Effectiveness of Chlorine Dioxide in Phosphate Mixture Against *Candida albicans*

Materials:

1. Purogene (2% chlorine dioxide), lot #8907:41, manufactured by BIO-CIDE International, Inc., P.O. Box 2700, Norman, Okla. 73070.
2. Test Organism: Candida albicans (ATCC#18804)
3. Saline, 0.9% NaCl.
4. Butterfield's Buffer phosphate dilutent (BFB), pH 7.2.

TABLE I

RESULTS SHOWING THE STABILITY OF CHLORINE DIOXIDE SOLUTION AT pH 6.8 IN DISTILLED WATER AND 1% SODIUM PHOSPHATE, MONOBASIC, DIBASIC, AND TRIBASIC

		DAY									
	Theroetical	0		7		14		21		28	
SOLUTION	% ClO_2	pH	% ClO_2	pH	% ClO_2	pH	% ClO_2	pH	% ClO_2	pH	% ClO_2
Distilled Water	0.02	6.8	0.02	6.9	0.02	6.9	0.02	6.5	0.02	6.5	0.02
	0.05	6.8	0.05	6.9	0.05	6.9	0.05	7.1	0.05	6.9	0.05
	0.1	6.8	0.1	6.9	0.1	7.0	0.1	7.7	0.1	7.6	0.1
	0.2	6.8	0.2	6.9	0.2	6.9	0.2	7.2	0.2	7.2	0.2
1% Na_2HPO_4	0.02	6.8	0.02	6.1	0.02	6.7	0.02	6.7	0.02	6.8	0.02
(Disodium	0.05	6.8	0.05	6.8	0.05	6.8	0.05	6.8	0.05	6.8	0.05
hydrogen phosphate)	0.1	6.8	0.1	6.9	0.1	6.9	0.1	6.8	0.1	6.8	0.1
	0.2	6.8	0.2	6.9	0.2	6.9	0.2	6.9	0.2	6.8	0.2
NaH_2PO_4	0.02	6.8	0.02	6.7	0.02	6.8	0.02	6.7	0.02	6.8	0.02
(Sodium	0.05	6.8	0.05	6.8	0.05	6.8	0.05	6.8	0.05	6.9	0.05
dihydrogen	0.1	6.8	0.1	6.8	0.1	6.8	0.1	6.9	0.1	6.9	0.1
phosphate)	0.2	6.8	0.2	6.8	0.2	6.8	0.2	6.9	0.2	6.9	0.2
1% Na_3PO_4	0.02	6.8	0.02	6.8	0.02	6.4	0.02	6.9	0.02	7.0	0.02
(Trisodium	0.05	6.8	0.05	7.0	0.05	7.1	0.05	6.9	0.05	7.0	0.05
phosphate)	0.1	6.8	0.1	7.5	0.1	7.5	0.1	7.0	0.1	6.9	0.1
	0.2	6.8	0.2	7.0	0.2	7.1	0.2	6.9	0.2	6.9	0.2

EXAMPLE 2

The stability of Chlorine Dioxide at Ph 6.8 in the Presence of 0.2% Phosphate

The following is an example of how to test the stability of chlorine dioxide at pH 6.8 in the presence of 0.2% phosphate.

Materials:

1. Purogene (2% $C10_2$), Lot #8907.41, 1 gallon, Manufactured by BIO-Cide, International, P.O. Box 2700, Norman, Okla. 73070.
2. Sodium Phosphate, monobasic, dibasic, and tribasic.

Methods:

A 0.2% solution of monobasic sodium phosphate is prepared in distilled water. Ten ml is placed into each of four beakers. One of each of the four beakers receives 1, 2.5, 5, and 10 ml of chlorine dioxide concentrate (2% $C10_2$), respectively. All solutions were diluted to 90 ml with distilled water, adjusted to pH 6.8 with 1 N NaOH and 1 N HCl, diluted to 100 ml and placed in screw cap bottles.

5. Sterile 15% sodium thiosulfate.
6. Blood agar.
7. Stop watch.
8. Sterile 1 N HCl and 1 N NaOH.
9. pH meter.
10. McFarland nephelometer tube No. 1. Density of this tube is equivalent to a bacterial suspension of 3×108 organisms per ml.
11. N,N-diethyl-p-phenylenediamine (DPD reagent).
12. Phosphate buffer reagent.
13. Sodium dihydrogen phosphate, $NaH_2PO_4.7H_2O$.
14. Trisodium phosphate, $Na_3PO_4.12H_2O$.
15. Sodium monofluorophosphate, $Na_2FPO.$, Ref No. OB 12837, manufactured by Albright and Wilson, P.O. Box 80, Oldbury, Narley, West Midlands, B694LN, England.

DPD reagent and phosphate buffer reagent were prepared in accord with Standard Methods for the Examination of Water and Wastewater, 17th Edition, p. 9–54 (1989).

Methods:

1. Test Solutions:

A ten percent sodium dihydrogen phosphate solution was prepared in distilled water. Ten ml was placed into each of five beakers. One of each of the five beakers received 0, 1, 2.5, 5, and 10 ml of chlorine dioxide concentrate (2% $C10_2$), respectively. All solutions were diluted to 90 ml with distilled water, adjusted to pH 6.0 with 1 N NaOH and 1 N HCl, diluted to 100 ml and placed in screw cap bottles. Solutions containing 0 ppm chlorine dioxide were filter sterilized prior to use.

Solutions containing trisodium phosphate and sodium monofluorophosphate were prepared in a similar manner.

II. Test Suspensions:

Suspensions of the *Candida albicans* organism were prepared in Butterfield's buffer from 48 hour agar cultures and turbidity adjusted to a McFarland Tube #1. Subsequently 0.1 ml of this suspension was diluted in 50 ml of saline. The diluted microorganism suspensions were now ready for use.

III. Test Procedure:

1. Test:

One ml of test suspension was aliquoted into each of five sterile 16×125 mm screw cap tubes. Each of the five tubes received 4 ml of a solution containing either 0, 200, 500, 1000, or 2000 ppm chlorine dioxide in 1% sodium dihydrogen phosphate. Each tube was shaken for ten seconds and immediately inactivated with 0.25 ml 15% sodium thiosulfate. Solutions containing 1% trisodium phosphate and 1% sodium monofluorophosphate were handled in a similar manner.

2. Controls:

One ml of test suspension was dispensed into two sterile 16×125 mm screw cap tubes. Each tube received 4 ml 2000 ppm chlorine dioxide in 1% sodium dihydrogen phosphate. The first tube received 0.25 ml sodium thiosulfate, while the second tube received none. Subsequently each tube was tested for residual chlorine dioxide by adding 0.3 ml phosphate buffer reagent and 0.3 ml DPD reagent to each tube. Neutralized tubes were colorless, while nonneutralized tubes were pink. Solutions of trisodium phosphate and sodium monofluorophosphate containing 2,000 ppm chlorine dioxide were handled in a similar manner.

One ml test suspension of the *Candida albacans* organism was treated with 4 ml Butterfield's buffer and 0.25 ml 10% sodium thiosulfate as a negative control.

After inactivation with sodium thiosulfate all tubes were plate counted.

Sterility tests on all reagents were run parallel to experiments by plate counted method. The plate counted method and sterility tests were conducted in accord with Standard Methods for the Examination of Water and Wastewater, 17th Edition, p. 9–54 (1989).

Results and Summary:

As shown in Table 2, 99–100% of the *Candida albicans* organisms were killed when challenged with 1,000 ppm (0.1%)–2,000 ppm (0.2%) chlorine dioxide in either 1% sodium dihydrogen phosphate or trisodium phosphate. Chlorine dioxide concentrations of 200 (0.02%) and 500 ppm (0.05%) in the presence of phosphates demonstrated marginal bacteriocidal activity against *C.albicans* (39–51% kill).

TABLE 2

RESULTS SHOWING THE BACTERIOCIDAL ACTIVITY OF CHLORINE DIOXIDE IN PHOSPHATE SOLUTIONS AT pH 6.0 AGAINST CANDIDA ALBICANS

	PHOSPHATE SOLUTION		
CLO_2 (PPM)	Negative Control*	1% NaH_2HPO_4	1% Na_2PO_4
0	95,000**	64,000 (33)***	55,000 (42)
200	ND	58,000 (39)	64,000 (33)
500	ND	47,000 (51)	32,000 (66)
1000	ND	250 (99)	0 (100)
2000	ND	17 (99)	5 (99)

*Butterfield's buffer
**Organisms/ml
***Percent Kill
ND = Not Done

EXAMPLE 4

The Effectiveness of Chlorine Dioxide in Phosphate Mixture Against *Candida albicans* in the Presence and Absence of Serum

Materials:

1. Purogene, Lot #8907:41, 1 gallon (contains 2% $C10_2$), manufactured by BIO-CIDE International; Inc., P.O. Box 2700, Norman, Okla. 73070.
2. Test Organism: Candida albicans (ATCC #18804) obtained from American Type Culture Collection, (ATCC) 12301 Parklawn Drive, Rockville, Md. 20852.
3. 15% Sodium thiosulfate ($Na_2S_2O_3$)
4. Plate Count agar
5. Newborn calf serum, Colostrum free, Lot #30P7485, Gibco Laboratories, Grand Island, N.Y., 14072.
6. Butterfield's Buffer, pH 7.2
7. Trisodium phosphate, $Na_3PO_4.12H_2O$, Sigma Chemical Co., St. Louis Mo. 63178.

Methods:

Chlorine dioxide solution having concentrations of 0, 200, 500, 1,000 and 2,000 mg/L were prepared from Purogene concentrate. Each $C10_2$ concentration was prepared to contain 0.5% tribasic sodium phosphate (i.e., trisodium phosphate, $Na_3PO_4.12H_2O$). In a similar manner, chlorine dioxide solutions of 0, 200, 500, 1,000 and 2,000 mg/L were prepared, with each solution containing 1.0% tribasic sodium phosphate. The pH of the chlorine dioxide/phosphate mixture was adjusted to 6.5 with 1 N and 6 N hydrochloric acid.

Tryptic Soy Broth (100 ml) was innoculated with *Candida albicans* and incubated 24 hours at 35° C. After incubation, the cells were washed three times with Butterfield's buffer and resuspended in 100 ml buffer.

Testing in the absence of Serum:

Chlorine dioxide-phosphate solutions (100 ml) were dispensed into sterile 16×125 mm screw cap tubes, 9 ml/tube. Three tubes were prepared for each $C10_2$ concentration. One ml of washed *C. albicans* suspension was added to one tube of each $C10_2$ concentration, and mixed vigorously for 10 seconds. One minute after addition of $C10_2$, 2 ml of 15% sodium thiosulfate ($Na_2S_2O_3$) was added to each tube and well mixed to inactivate the mixture. The procedure was repeated twice with the remaining tubes except that $C10_2$ was inactivated with sodium thiosulfate after 2 and 5 minutes respectively.

Serial ten-fold dilutions (10^{-1}–10^{-5}) of *Candida albicans*/ClO_2 mixtures were prepared in Butterfield's buffer. Simultaneously, one ml of each dilution was transferred to a sterile 15 mm petri dish. Then 10 ml of plate count agar at 45–47° C. was added to each plate, and the plates were swirled and allowed to solidify. Plates were inverted and incubated 76 hours at 35° C., and colonies counted.

Testing in Presence of Serum:

Chlorine dioxide-phosphate solutions, were aliquoted, 8 ml/tube. Three tubes were prepared per ClO_2 concentration. Fifty ml washed *C. albicans* suspension was added with 50 ml newborn calf serum. 2 ml of the serum-*C. albicans* suspension was added to test tubes and processed as described above.

Results:

Results showing percent kill of *Candida albicans* as a result of application of chlorine dioxide-phosphate solutions are shown in Tables 3 and 4.

TABLE 3

Results Showing Bacteriocidal Activity of Chlorine Dioxide-Phosphate (0.5%) Solutions at pH 6.5 Against Candida Albicans

TIME	ClO_2 w/out Serum (ppm)				ClO_2 w/Serum (ppm)			
(Seconds)	200	500	1000	2000	200	500	1000	2000
1	33*	44	99+	99+	<10	27	18	36
2	13	33	99+	99+	40	30	30	30
5	29	35	99+	99+	13	<10	<10	ND

*Percent kill
ND = Not done
+ = greater than

TABLE 4

Results Showing Bacteriocidal Activity of Chlorine Dioxide-Phosphate (1%) Solutions at pH 6.5 Against Candida Albicans

TIME	ClO_2 w/out Serum (ppm)				ClO_2 w/Serum (ppm)			
(Seconds)	200	500	1000	2000	200	500	1000	2000
1	30*	65	99+	99+	<10	10	<10	<10
2	37	47	99+	99+	19	<10	29	19
5	17	ND	99+	99+	<10	<10	<10	<10

*Percent kill
ND = Not done
+ = greater than

EXAMPLE 5

The Effectiveness of Chlorine Dioxide in Phosphate Mixture Against Actinobacillus Actinomycetemcomitans in the Presence and Absence of Serum

Materials:

1. Purogene, Lot #8907:41, 1 gallon (contains 2% ClO_2), manufactured by BIO-CIDE International, Inc., P.O. Box 2700, Norman, Okla. 73070.
2. *Actinobacillus actinomycetemcomitans*, ATCC #29522, obtained from American Type Culture Collection, 12301, Parklawn Drive, Rockville, Md. 20852.
3. 15% Sodium thiosulfate ($Na_2S_2O_3$)
4. Plate Count agar
5. Newborn calf serum, Colostrum free, Lot #30P7485, Gibco Laboratories, Grand Island, N.Y., 14072.
6. Butterfield's Buffer, pH 7.2
7. Trisodium phosphate, $Na_3PO_4.12H_2O$, Sigma Chemical Co., St. Louis Mo. 63178

Methods:

Chlorine dioxide solutions having concentrations of 1,000 and 2,000 mg/L were prepared from Purogene concentrate. Each ClO_2 concentration was prepared to contain 0.2% sodium phosphate, tribasic (i.e., trisodium phosphate, $Na_3PO_4.12H_2O$). The pH of the chlorine dioxide/phosphate mixture was adjusted to 6.5 with 1 N hydrochloric acid.

Three chocolate agar plates were inoculated with *Actinobacillus actinomycetemcomitans* and incubated 48 hours at 35° C. in a candle jar. After incubation, cells were scraped from the plates with a cotton swab and suspended in 100 ml buffer. 50 ml of this suspension was diluted with 50 ml buffer, while the other 50 ml was diluted with 50 ml serum.

Testing in the absence of Serum:

Chlorine dioxide-phosphate solutions (100 ml) were dispensed into sterile 150 ml beakers containing magnetic stir bars. While stirring on a magnetic mixer, a 10 ml portion of *A. actinomycetemcomitans*—buffer suspension was added. At 10, 30 and 60 second intervals, 10 ml was removed from the beaker and transfered to a 16×125 mm tube which contained 2 ml 15% sodium thiosulfate. The tube was capped, mixed, and a plate count was performed employing chocolate agar as the growth media, in accord with the methods described in *FDA Bacteriological Analytical Manual,* 6th edition, 1984, chapters 4, 17, herein incorporated by reference.

Testing in Presence of Serum:

Testing in the presence of serum was handled in a similar manner, except that an *Actinobacillus actinomycetemcomitans*-serum suspension was subtituted for the *Actinobacillus actinomycetemcomitans*-buffer suspension.

Results:

Results showing percent kill of *Actinobacillus actinomycetemcomitans* following application of the chlorine dioxide-phosphate solutions are shown in Table 5.

TABLE 5

Results Showing Bacteriocidal Activity of Chlorine Dioxide-Phosphate (0.2%) at pH 6.5 Against Actinobacillus Actinomycetemcomitans

TIME	ClO_2 w/out Serum (ppm)		ClO_2 w/ Serum (ppm)	
(Seconds)	1000	2000	1000	2000
10	99*	99+	99+	99+
30	99+	99+	99+	99+
60	99+	99+	99+	99+

*Percent kill
+ = greater than

EXAMPLE 6

The Effectiveness of Chlorine Dioxide in Phosphate Mixture Against *Porphyromonas gingivalis* in the Presence and Absence of Serum

Materials:

1. Purogene, Lot #8907:41, 1 gallon (contains 2% ClO_2), manufactured by BIO-CIDE International, Inc., P.O. Box 2700, Norman, Okla. 73070.
2. *Porphyromonas* (formerly known as Bacteroides) *gingivalis*, ATCC # 33277, obtained from American Type Culture Collection, 12301 Parklawn Drive, Rockville, Md. 20852.

3. 15% Sodium thiosulfate ($Na_2S_2O_3$)
4. Plate Count agar
5. Newborn calf serum, Colostrum free, lot #30P7485, Gibco Laboratories, Grand Island, N.Y., 14072.
6. Butterfield's Buffer, pH 7.2
7. Trisodium phosphate, $Na_3PO_4.12H_2O$, Sigma Chemical Co., St. Louis Mo. 63178.

Methods:

Chlorine dioxide solutions having concentrations of 1,000 and 2,000 mg/L were prepared from Purogene concentrate. Each ClO_2 concentration was prepared to contain 0.2% sodium phosphate, tribasic (i.e., trisodium phosphate, $Na_3PO_4.12H_2O$). The pH of the chlorine dioxide/phosphate mixture was adjusted to 6.5 with 1 N hydrochloric acid. Three anaerobic BAP plates were inoculated with *gingivalis* (ATCC 33277) and incubated 72 hours at 35° C. After incubation, cells were scraped from the plates with a cotton swab and suspended in 100 ml buffer. 50 ml of this suspension was diluted with 50 ml buffer, while the other 50 ml was diluted with 50 ml serum.

Testing in the Absence of Serum:

Chlorine dioxide-phosphate solutions (100 ml) were dispensed into sterile 150 ml beakers containing magnetic stir bars. While stirring on a magnetic mixer, a 10 ml portion of *P.gingivalis*-buffer suspension was added. At 10, 30 and 60 second intervals, 10 ml was removed from the beaker and transferred to a 16×125 mm tube which contained 2 ml 15% sodium thiosulfate. Tube was capped, mixed, and an anaerobic plate count was performed using anaerobic blood agar in accord with the methods described in *FDA Bacteriological Analytical Manual,* 6th edition, 1984, chapter 17.

Testing in Presence of Serum:

Testing in the presence of serum was handled in a similar manner to that described immediately above, except that a *Porphyromonas gingivalis*-serum suspension was substituted for the *Porphyromonas gingivalis*-buffer suspension.

Results:

Results showing percent kill of *Porphyromonas gingivalis* by application of chlorine dioxide-phosphate solutions are shown in Table 6.

TABLE 6

Results Showing Bacteriocidal Activity of Chlorine Dioxide-Phosphate (0.2%) Solutions at pH 6.5 Against Porphyromonas Gingivalis

TIME	ClO_2 w/out Serum (ppm)		ClO_2 w/ Serum (ppm)	
(Seconds)	1000	2000	1000	2000
10	89*	99+	82	86
30	99+	99+	84	97
60	99+	99+	94	99

*Percent kill
+ = greater than

EXAMPLE 7

A boy diagnosed as having Thrush was treated with the drug ketonideozole for two weeks. The Candida were not controlled. The boy was then treated with a mouthrinse solution and toothpaste both of which contained as the effective ingredient a composition comprising 0.1% chlorine dioxide together with 0.2% trisodium phosphate. The boy's Thrush infection was brought under control within 3 days. The treating pediatrician was surprised and did not understand how the boy's recovery could happen so quickly.

EXAMPLE 8

The present inventor has treated hairy leukoplakia present on the tongue of AIDS-infected patients. The daily use of a toothpaste and mouthrinse, both of which contained as the effective ingredient a composition comprising 0.1% chlorine dioxide together with 0.2% trisodium phosphate, resulted in the disappearance of the hairy leukoplakia within 14 days. When the chlorine dioxide/phosphate-containing products were withdrawn, the hairy leukoplakia returned within 14 days. When the same products were again administered, the hairy leukoplakia again disappeared.

EXAMPLE 9

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the vagina of a patient afflicted with vaginitis. It is predicted that the patient will experience a cessation of vaginitis symptoms as a result of the regular administration of the composition.

EXAMPLE 10

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the vagina of a patient affiicted with leukoplakia vulvae. It is predicted that the patient will experience a cessation of the leukoplakia vulvae symptoms as a result of the regular administration of the composition.

EXAMPLE 11

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the urethra of a patient infected in that orifice with *Actino-*

bacillus actinomycetemcomitans. It is predicted that the patient will experience a cessation of symptoms of the infection as a result of the regular administration of the composition.

EXAMPLE 12

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the vagina of a patient infected in that orifice with *Porphyromonas gingivalis*. It is predicted that the patient will experience a cessation of symptoms of the infection as a result of the regular administration of the composition.

EXAMPLE 13

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the rectum of a patient infected in that orifice with *Porphyromonas gingivalis*. It is predicted that the patient will experience a cessation of symptoms of the infection as a result of the regular administration of the composition.

EXAMPLE 14

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the auditory canal of a patient infected in that orifice with *Actinobacillus actinomycetemcomitans*. It is predicted that the patient will experience a cessation of symptoms of the infection as a result of the regular administration of the composition.

EXAMPLE 15

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the nasal canal of a patient infected in that orifice with *Porphyromonas gingivalis*. It is predicted that the patient will experience a cessation of symptoms of the infection as a result of the regular administration of the composition.

EXAMPLE 16

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	at least 0.1%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the ocular canal of a patient infected in that orifice with *Actinobacillus actinomycetemcomitans*. It is predicted that the patient will experience a cessation of symptoms of the infection as a result of the regular administration of the composition.

EXAMPLE 17

Hypothetically, the following composition may be prepared:

Stabilized chlorine dioxide	1.0–2.0%
Phosphate compound	at least 0.05%

Preferable phosphate compounds include disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate, in particular trisodium phosphate or sodium monofluorophosphate.

The above composition may be applied on a daily basis to the bodily orifices of a severely immunocompromised patient afflicted with leukoplakia, and with opportunistic bacterial and fungal infections. It is predicted that the patient will experience a cessation of leukoplakia and symptoms of infection as a result of the regular administration of the composition.

EXAMPLE 18

A secretary in the employ of the present inventor developed a vaginitis. She called for an appointment with her gynecologist only to learn that she could not be seen for

several days. Because of the extreme itching, and knowing, as a consequence of her employment with the present inventor, that activated chlorine dioxide would kill Candida, she of her own initiation and volition used as a douche a mouthrinse developed by the present inventor, which mouthrinse contains 0.1% activated chlorine dioxide and 0.2% trisodium phosphate. She reported that she was asymptomatic immediately upon application of the above composition, with no itching. She took a wet cloth and applied the above composition locally, in the vicinity of the vagina, for three or four days, with no recurrent symptoms.

In the practice of methods to use the compounds of the present invention, an effective amount of the chlorine dioxide/phosphate composition is administered to the subject in need of, or desiring, such treatment. These compounds or compositions may be administered by any of a variety of routes depending upon the specific end use, including topically, as a lotion, creme or solution, by lavage, suppository, or as a nasal drop or spray.

The most suitable route in any given case will depend upon the use, particular active ingredient, the subject involved, and the judgment of the medical practitioner.

A further aspect of the present invention relates to pharmaceutical compositions containing as active ingredients a compound of the present invention which compositions comprise such compound in admixture with a pharmaceutically acceptable, nontoxic carrier. As mentioned above, such compositions may be prepared for use for topical application, particularly in the form of liquid solutions, suspensions, semi-solids, salves or creams, suppositories, or intranasally particularly in the form of nasal drops or aerosols.

It will be readily apparent to those skilled in the art that a number of modifications and changes can be made without departing from the spirit and scope of the present invention. Therefore, it is not intended that the invention be limited by the illustrative examples but only by the claims which follow.

I claim:

1. A topical composition for treating conditions of the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices, brought about by the occurrence of any of fungal and bacterial infections, leukoplakia, penetration of bacterial toxins, living unicellular microorganisms, vaginitis, endometriosis, *Porphyromonoas gingivalis, Actinobacillus actinomycetemcomitans*, Pseudomonades, Candid species and leukoplakia vulvae, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains chlorine dioxide in a concentration in the range of about 0.005% to about 2.0% and a phosphate compound comprising trisodium phosphate, wherein the concentration of the phosphate compound is in a range of about 0.02% to about 3.0% to retard escape of the chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

2. A topical composition treating conditions of the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices, brought about by the occurrence of any of fungal and bacterial infections, leukoplakia, penetration of bacterial toxins, living unicellular microorganisms, vaginitis, endometriosis, *Porphyromonoas gingivalis, Actinobacillus actinomycetemcomitans*, Pseudomonades, Candida species and leukoplakia vulvae, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains chlorine dioxide in a concentration in the range of about 0.005% to about 2.0% and a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate or sodium monofluorophosphate, wherein the concentration of the phosphate compound is in a range of about 0.02% to about 3.0% to retard escape of chlorine dioxide from said topical preparation said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

3. The composition as set forth in claim **1**, wherein the phosphate compound is sodium monofluorophosphate.

4. The composition as set forth in claim **1**, wherein the concentration of the chlorine dioxide is about 0.2% and the concentration of the phosphate compound is about 1.0%.

5. A topical composition for treating conditions of the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices, brought about by the occurrence of any of fungal and bacterial infections, leukoplakia, penetration of bacterial toxins, living unicellular microorganisms, vaginitis, endometriosis, *Porphyromonoas gingivalis, Actinobacillus actinomycetemcomitans*, Pseudomonades, Candida species and leukoplakia vulvae, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains a concentration of at least 0.1% chlorine dioxide and a concentration of at least 0.05% of a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate to retard escape of the chlorine dioxide from said topical preparation- said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

6. The composition as set forth in claim **5**, wherein the phosphate compound is sodium monofluorophosphate.

7. A topical composition treating conditions of the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices, brought about by the occurrence of any of fungal and bacterial infections, leukoplakia, penetration of bacterial toxins, living unicellular microorganisms, vaginitis, endometriosis, *Porphyromonoas gingivalis, Actinobacillus actinomycetemcomitans*, Pseudomonades, Candida species and leukoplakia vulvae, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains a concentration of at least 0.005% chlorine dioxide and a concentration of at least 0.02% of a phosphate compound comprising trisodium phosphate to retard escape of the chlorine dioxide from said topical preparation said total preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

8. A topical composition for treating the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices by reducing the number of bacteria, including *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis*, in the orifices, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains

chlorine dioxide in a concentration in the range of about 0.005% to about 2.0% and a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate in a concentration in the range of about 0.02% to about 3.0% to retard escape of chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

9. A topical composition for treating the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices by reducing the number of bacteria, including *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis*, in the orifices, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains a concentration of at least 0.1% chlorine dioxide and a concentration of at least 0.05% of a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate to retard escape of chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

10. A topical composition for treating the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices by reducing the occurrence of leukoplakia in the orifices, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains chlorine dioxide in a concentration in the range of about 0.005% to about 2.0% and a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate in a concentration in the range of about 0.02% to about 3.0% to retard escape of chlorine dioxide from said topical preparation, said tropical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

11. A topical composition for treating the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices by reducing the occurrence of leukoplakia in the orifices, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains a concentration of at least 0.1% chlorine dioxide and a concentration of at least 0.05% of a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate to retard escape of chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

12. A topical composition for treating the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices by reducing the number of yeasts including *Candida albicans* in the orifices, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains chlorine dioxide in a concentration in the range of about 0.005% to about 2.0% and a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate in a concentration in the range of about 0.02% to about 3.0% to retard escape of chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

13. A topical composition for treating the epithelium of the rectal, vaginal, urethral, oral, nasal, ocular, and auditory canal orifices by reducing the number of yeasts including *Candida albicans* in the orifices, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories, wherein said topical preparation contains a concentration of at least 0.1% chlorine dioxide and a concentration of at least 0.05% of a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate to retard escape of chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

14. A composition for treating vaginitis and endometriosis by reducing any of Candida, *Actinobacillus actinomycetemcomitans*, Pseudomonades, and *Porphyromonas gingivalis* bacteria present in the vagina or the uterus, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories to be applied to the vagina or the uterus, wherein said topical preparation contains chlorine dioxide in a concentration in the range of about 0.005% to about 2.0% and a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate in a concentration in the range of about 0.02% to about 3.0% to retard escape of chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

15. A topical composition for treating vaginitis and endometriosis by reducing any of Candida, *Actinobacillus actinomycetemcomitans*, Pseudomonades, and *Porphyromonas gingivalis* bacteria present in the vagina or the uterus, said composition comprising a topical preparation selected from the group consisting of liquid solutions, suspensions, semi-solids, salves, creams, and suppositories to be applied to the vagina or the uterus, wherein said topical preparation contains chlorine dioxide in a concentration of at least 0.1% and a phosphate compound selected from the group consisting of disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, or sodium monofluorophosphate in a concentration of at least 0.05% to retard escape of chlorine dioxide from said topical preparation, said topical preparation being at a pH in the range of about 6.0 to about 7.4, thereby increasing the shelf life and efficacy of said topical preparation.

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